Amendments to the Claims

This listing of the claims replaces all prior versions of the claims in the application:

Listing of the Claims:

1.-64. (Cancelled)

65. (Currently Amended) An implantable biocompatible cell device, the device comprising:

i) a semipermeable membrane permitting the diffusion of a ~~protein~~ polypeptide comprising an amino acid sequence selected from the group consisting of:

A) the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24;

B) a sequence variant having at least 80 % identity to the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24; and

C) a biologically active fragment of at least 50 contiguous amino acids of any of A) through B),

~~as defined by any of the preceding claims 1 to 21 and/or~~, a virus vector, or both; and

ii) a ~~composition of~~ core containing cells ~~according to any of the claims 56 to 62~~ transformed or transduced with a vector comprising a nucleic acid molecule encoding a polypeptide or its complementary sequence, said polypeptide comprising an amino acid sequence selected from the group consisting of:

D) the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24;

E) a sequence variant having at least 80 % identity to the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24; and

F) a biologically active fragment of at least 50 contiguous amino acids of any of D) through E),

or a packaging cell line ~~according to any of the claims 63 to 64~~ capable of producing an infective virus particle, said virus particle comprising a Retroviridae-derived genome

comprising a 5' retroviral LTR, a tRNA binding site, a packaging signal, a promoter operably linked to a polynucleotide sequence encoding a polypeptide comprising an amino acid sequence selected from the group consisting of:

G) the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24;

H) a sequence variant having at least 80 % identity to the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24; and

I) a biologically active fragment of at least 50 contiguous amino acids of any of G) through H),

an origin of second strand DNA synthesis, and a 3' retroviral LTR.

66. (Original) The device of claim 65, wherein the semipermeable membrane is immunoisolatory.

67. (Original) The device of claim 65, wherein the semipermeable membrane is microporous.

68. (Original) The device of claim 65, wherein the device further comprises a matrix disposed within the semipermeable membrane.

69. (Original) The device of claim 65, wherein the device further comprises a tether anchor.

70. (Currently Amended) The device of claim 65, wherein said ~~device comprises a~~ core comprises ~~comprising~~ living packaging cells that secrete a viral vector for infection of a target cell, wherein the viral vector is a retrovirus, wherein ~~the vector comprising a heterologous gene encoding a polypeptide according to any of claims 1 to 21, operably linked to a~~ the promoter ~~that~~ regulates the expression of said polypeptide in the target cell~~; and an external jacket surrounding said core~~, ~~said jacket comprising~~ and wherein said semipermeable membrane comprises a permeable biocompatible material, said material having a porosity

selected to permit passage of retroviral vectors of approximately 100 nm diameter thereacross, thereby permitting release of said viral vector from said ~~capsule~~ device.

71. (Currently Amended) The device of claim 70, wherein the core additionally comprises a matrix[[,]] and the packaging cells ~~being~~ are immobilized by the matrix.

72. (Currently Amended) The device of claim 70, wherein the semipermeable membrane ~~jacket~~ comprises a hydrogel or thermoplastic material.

73.-88. (Cancelled)

89. (Currently Amended) A method of treatment of a pathological condition in a subject comprising administering to an individual in need thereof a therapeutically effective amount of:

i) ~~the~~ a polypeptide ~~of any of the claims 1 to 21~~ comprising an amino acid sequence selected from the group consisting of:

A) the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24;

B) a sequence variant having at least 80 % identity to the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24; and

C) a biologically active fragment of at least 50 contiguous amino acids of any of A) through B); or

ii) ~~the~~ an isolated nucleic acid sequence ~~of any of the claims 22 to 50~~ encoding the polypeptide described in i); or

iii) ~~the~~ an expression vector ~~of any of the claims 51 to 55~~ comprising the isolated nucleic acid molecule described in ii); or

iv) a composition of host cells ~~according to any of the claims 56 to 62~~ transformed or transduced with the vector described in iii); or

v) an implantable biocompatible cell device according to ~~any of the~~ claim[[s]] 65 ~~72~~; or

vi) a packaging cell line ~~according to any of the claims 63 to 64~~ capable of producing an infective virus particle, said virus particle comprising a Retroviridae-derived genome comprising a 5' retroviral LTR, a tRNA binding site, a packaging signal, a promoter operably linked to a polynucleotide sequence encoding the polypeptide described in i), an origin of second strand DNA synthesis, and a 3' retroviral LTR.

90. (Original) The method of claim 89, wherein the pathological condition is an immunological disorder.

91 (Currently Amended) The method of claim 90, wherein the immunological disorder is selected from the group consisting of: infectious diseases, immune deficiencies, cancer, autoimmune disorders, ~~including~~ multiple sclerosis, allergic reactions and conditions, and graft-versus-host disease.

92. (Currently Amended) The method of claim 89, wherein said ~~medicament~~ pathological condition is ~~for the treatment of~~ a disease, disorder, or damage associated with the nervous system.

93. (Currently Amended) The method of claim 92, wherein said ~~medicament is for the treatment of a~~ disease, disorder, or damage associated with the nervous system ~~involving~~ involves injury to the brain, brain stem, the spinal cord, ~~and/or~~ peripheral nerves, or a combination thereof ~~including but not limited to~~ or is selected from the group consisting of ~~conditions such as~~ stroke, traumatic brain injury, spinal cord injury, diffuse axonal injury, epilepsy, neuropathy, peripheral neuropathy and associated pain, and other symptoms.

94. (Currently Amended) The method of claim 92, wherein the disease, disorder, or damage associated with the ~~N~~nervous ~~S~~system ~~disorder~~ involves degeneration of neurons and their processes in the brain, brain stem, the spinal cord, ~~and/or~~ the peripheral nerves, or a combination thereof, ~~including but not limited to~~ or is selected from the group consisting of Parkinson's Disease, Alzheimer's Disease, senile dementia, Huntington's Disease, amyotrophic lateral sclerosis, neuronal injury associated with multiple sclerosis, and

associated symptoms.

95.-97. (Cancelled)

98. (Currently Amended) The method of claim 92, wherein the disease, disorder, or damage associated with the nervous system ~~disorder is a disease, disorder, or damage involving~~ involves dysfunction ~~and/~~or loss or both of neurons in the brain, brain stem, the spinal cord, ~~and/or~~ the peripheral nerves, or a combination thereof, or is selected from the group consisting of~~, including but not limited to~~ conditions caused by metabolic diseases, ~~nutiritional~~ nutritional deficiency, toxic injury, malignancy, ~~and/or~~ genetic or idiopathic conditions~~, including but not limited to~~ diabetes, renal dysfunction, alcoholism, chemotherapy, chemical agents, drug abuse, vitamin deficiency, ~~and~~ infection, and combinations thereof.

99. (Original) The method of claim 98, wherein the disease is peripheral neuropathy and associated pain.

100. (Currently Amended) The method of claim 92, wherein the disease, disorder, or damage associated with the nervous system ~~disorder is a disease, disorder, or damage involving~~ involves degeneration or sclerosis of glia, ~~such as~~ oligodendrocytes, astrocytes ~~and~~ or Schwann cells in the brain, brain stem, the spinal cord, ~~and~~ the peripheral nerves, or a combination thereof, or is selected from the group consisting of ~~including but not limited to~~ multiple sclerosis, optic neuritis, cerebral sclerosis, post-infectious encephalomyelitis, and epilepsy and associated symptoms.

101. (Currently Amended) The method of claim 100, wherein the disease or disorder is selected from the group consisting of multiple sclerosis, sensory ataxus, neurodegenerative spinocerebellar disorders, hereditary ataxis, cerebellar atrophies, and alcoholism.

102. (Currently Amended) The method of claim 92, wherein the disease, disorder, or damage associated with the nervous system ~~disorder is a disease, disorder, or damage~~

involves the retina, photoreceptors, ~~and~~ associated nerves, or a combination thereof, or is selected from the group consisting of ~~including but not limited to~~ retinitis pigmentosa, macular degeneration, glaucoma, diabetic retinopathy, and associated symptoms.

103. (Currently Amended) The method of claim 92, wherein disease, disorder, or damage associated with the nervous system ~~disorder is a disease, disorder, or damage~~ involves the sensory epithelium ~~ans~~ and associated ganglia of the vestibuloacoustic complex or is selected from the group consisting of ~~including but not limited to~~ noise-induced hearing loss, deafness, tinnitus, otitis, labyrintitis, hereditary and cochleovestibular atrophies, Menieres Disease, and associated symptoms.

104. (Original) The method of claim 89, wherein the subject is a human being.

105. (Currently Amended) A method of preventing apoptosis in a mammalian neuronal cell, said method comprising exposing said neuronal cell to a polypeptide ~~as defined in any of the claims 1 to 21~~ comprising an amino acid sequence selected from the group consisting of:

a) the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24;

b) a sequence variant having at least 80 % identity to the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24; and

c) a biologically active fragment of at least 50 contiguous amino acids of any of a) through b),

thereby preventing apoptosis in a mammalian neuronal cell.

106. (Currently Amended) A method of enhancing survival of a mammalian neuronal cell, said method comprising exposing said neuronal cell to a polypeptide ~~as defined in any of the claims 1 to 21~~ comprising an amino acid sequence selected from the group consisting of:

a) the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24;

b) a sequence variant having at least 80 % identity to the amino acid sequence

selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24; and

c) a biologically active fragment of at least 50 contiguous amino acids of any of a) through b),

thereby enhancing survival of a mammalian neuronal cell.

107. (Currently Amended) A method of generating a neuron, said method comprising exposing a neuronal precursor cell or a neuronal stem cell to a polypeptide ~~as defined in any of the claims 1 to 21~~ comprising an amino acid sequence selected from the group consisting of:

a) the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24;

b) a sequence variant having at least 80 % identity to the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24; and

c) a biologically active fragment of at least 50 contiguous amino acids of any of a) through b),

thereby generating a neuron.

108. (Currently Amended) A method of expanding a composition of mammalian cells, comprising administering to said composition the polypeptide ~~of any of the claims 1 to 21~~ comprising an amino acid sequence selected from the group consisting of:

a) the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24;

b) a sequence variant having at least 80 % identity to the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24; and

c) a biologically active fragment of at least 50 contiguous amino acids of any of a) through b);

or transducing/transfecting the cells with ~~the expression vector of any of the claims 51 to 55~~ an expression vector comprising a nucleic acid molecule encoding a polypeptide or its

complementary sequence, said polypeptide comprising an amino acid sequence selected from the group consisting of:

d) the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24;

e) a sequence variant having at least 80 % identity to the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24; and

f) a biologically active fragment of at least 50 contiguous amino acids of any of d) through e),

thereby expanding a composition of mammalian cells.

109. (Currently Amended) A method of differentiating a composition of mammalian cells, comprising administering to said composition the polypeptide ~~of any of the claims 1 to 21~~ comprising an amino acid sequence selected from the group consisting of:

a) the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24;

b) a sequence variant having at least 80 % identity to the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24; and

c) a biologically active fragment of at least 50 contiguous amino acids of any of a) through b);

or transducing/transfecting the cells with ~~the expression vector of any of the claims 51 to 55~~ an expression vector comprising a nucleic acid molecule encoding a polypeptide or its complementary sequence, said polypeptide comprising an amino acid sequence selected from the group consisting of:

d) the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24;

e) a sequence variant having at least 80 % identity to the amino acid sequence selected from the group consisting of SEQ ID No. 3, 4, 5, 8, 9, 10, 13, 14, 15, 19, 20, 21, 22, 23, and 24; and

f) a biologically active fragment of at least 50 contiguous amino acids of any of d)

through e),
thereby differentiating a composition of mammalian cells.

110.-112. (Cancelled)

113. (Currently Amended) An isolated polypeptide selected from the group consisting of AA_{128}-AA_{293} of SEQ ID No 3, AA_{121}-AA_{293} of SEQ ID No 3, AA_{129}-AA_{294} of SEQ ID No 8, AA_{122}-AA_{294} of SEQ ID No 8, AA_{126}-AA_{291} of SEQ ID No 13, AA_{119}-AA_{291} of SEQ ID No 13, and variants of said polypeptides, wherein any amino acid specified in the chosen sequence is changed to a different amino acid, provided that no more than 15 of the amino acid residues in the sequence are so changed.

114. (Original) The isolated polypeptide of claim 113, wherein the changed amino acids are selected from those designated as unconserved, weakly conserved or strongly conserved in Figure 3a.

115. (Original) An isolated polypeptide selected from the group consisting of SEQ ID No 19, 20, 21, 22, 23, and 24, and variant of said polypeptides, wherein any amino acid specified in the chosen sequence is changed to a different amino acid, provided that no more than 15 of the amino acid residues in the sequence are so changed.

116. (Original) The isolated polypeptide of claim 115, wherein the changed amino acids are selected from those designated as unconserved, weakly conserved or strongly conserved in Figure 3a.

117. (Original) An isolated polypeptide selected from the group consisting of:

i) AA_{30}-AA_{288} of SEQ ID No 3, and polypeptides having from one to five extra amino acids from the native sequence in one or both ends, up to AA_{25}-AA_{293} of SEQ ID No 3;

ii) AA_{28}-AA_{286} of SEQ ID No 13 and polypeptides having from one to five extra amino acids from the native sequence in one or both ends, up to AA_{23}-AA_{291} of SEQ ID No

13;

iii) AA_{31}-AA_{289} of SEQ ID No 8 and polypeptides having from one to five extra amino acids from the native sequence in one or both ends, up to AA_{26}-AA_{294} of SEQ ID No 8; and

iv) variants of said polypeptides, wherein any amino acid specified in the chosen sequence is changed to a different amino acid, provided that no more than 20 of the amino acid residues in the sequence are so changed.

118. (Currently Amended) An isolated polypeptide selected from the group consisting of:

i) AA_{171}-AA_{288} of SEQ ID No 3, and polypeptides having from one to five extra amino acids from the native sequence in one or both ends, up to AA_{165}-AA_{288}~~293~~ of SEQ ID No 3;

ii) AA_{169}-AA_{286} of SEQ ID No 13 and polypeptides having from one to five extra amino acids from the native sequence in one or both ends, up to AA_{164}-AA_{291} of SEQ ID No 13;

iii) AA_{172}-AA_{289} of SEQ ID No 8 and polypeptides having from one to five extra amino acids from the native sequence in one or both ends, ~~i.e.~~ up to AA_{167}-AA_{294} of SEQ ID No 8;

iv) variants of said polypeptides, wherein any amino acid specified in the chosen sequence is changed to a different amino acid, provided that no more than 10 of the amino acid residues in the sequence are so changed.

119. (Original) An isolated polypeptide selected from the group consisting of:

i) AA_{30}-AA_{118} of SEQ ID No 3, and polypeptides having from one to five extra amino acids from the native sequence in one or both ends, up to AA_{25}-AA_{123} of SEQ ID No 3;

ii) AA_{28}-AA_{116} of SEQ ID No 13 and polypeptides having from one to five extra amino acids from the native sequence in one or both ends, up to AA_{23}-AA_{121} of SEQ ID No 13;

iii) AA_{31}-AA_{119} of SEQ ID No 8 and polypeptides having from one to five extra amino acids from the native sequence in one or both ends, up to AA_{26}-AA_{124} of SEQ ID No 8; and

iv) variants of said polypeptides, wherein any amino acid specified in the chosen sequence is changed to a different amino acid, provided that no more than 10 of the amino acid residues in the sequence are so changed.

120. (Currently Amended) The polypeptide of claim 117~~, 118, or 119,~~ wherein the changed amino acids are selected from those designated as unconserved, weakly conserved or strongly conserved in Figure 3a.

121. (Currently Amended) An isolated polynucleotide coding for a polypeptide according to ~~any of the~~ claim[[s]] 113 ~~to 119~~.

122. (New) The polypeptide of claim 118, wherein the changed amino acids are selected from those designated as unconserved, weakly conserved or strongly conserved in Figure 3a.

123. (New) The polypeptide of claim 119, wherein the changed amino acids are selected from those designated as unconserved, weakly conserved or strongly conserved in Figure 3a.

124. (New) An isolated polynucleotide coding for a polypeptide according to claim 115.

125. (New) An isolated polynucleotide coding for a polypeptide according to claim 117.

126. (New) An isolated polynucleotide coding for a polypeptide according to claim 118.

127. (New) An isolated polynucleotide coding for a polypeptide according to claim 119.